Complete Summary

GUIDELINE TITLE

Guidelines for the management of spontaneous intracerebral hemorrhage in adults. 2007 update: a guideline from the American Heart Association/American Stroke Association Stroke Council, High Blood Pressure Research Council, and the Quality of Care and Outcomes in Research Interdisciplinary Working Group.

BIBLIOGRAPHIC SOURCE(S)

Broderick J, Connolly S, Feldmann E, Hanley D, Kase C, Krieger D, Mayberg M, Morgenstern L, Ogilvy CS, Vespa P, Zuccarello M, American Heart Association, American Stroke Association Stroke Council, High Blood Pressure Research Council, Quality of Care and Outcomes in Research Interdisciplinary Working Group. Guidelines for the management of spontaneous intracerebral hemorrhage in adults: 2007 update. Stroke 2007 Jun;38(6):2001-23. [204 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

It is intended that this guideline be fully updated in 3 years' time.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released.

- February 28, 2008, Heparin Sodium Injection: The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Spontaneous intracerebral hemorrhage

GUIDELINE CATEGORY

Diagnosis
Management
Prevention
Treatment

CLINICAL SPECIALTY

Cardiology
Critical Care
Emergency Medicine
Neurological Surgery
Neurology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To present current and comprehensive recommendations for the diagnosis and treatment of acute spontaneous intracerebral hemorrhage

TARGET POPULATION

Adults with spontaneous intracerebral hemorrhage

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Computed tomography
2. Magnetic resonance imaging

Treatment

1. Initial medical therapy
    - Monitoring and management in intensive care unit
    - Antiepileptic therapy
    - Antipyretic therapy
    - Early mobilization and rehabilitation for patients with ischemic stroke (as indicated)
    - Treatment of elevated intracranial pressure
    - Treatment of hyperglycemia (insulin)
    - Management of blood pressure
    - Recombinant activated factor VII (rFVIIa) (as part of a clinical trial only)
2. Prevention of deep vein thrombosis and pulmonary embolism
    - Pneumatic compression therapy
    - Treatment of hypertension
    - Heparin - low molecular weight, unfractionated
    - Vena cava filter
    - Long-term antithrombotic therapy
3. Management of coagulation and fibrinolysis
    - Protamine sulfate
    - Intravenous vitamin K
    - Prothrombin complex concentrate, factor IX complex concentrate, rFVIIa
    - Restarting antithrombotic therapy after antithrombotic therapy-related intracerebral hemorrhage (ICH)
    - Treatment of antithrombolytic therapy-related ICH
4. Surgical treatment of ICH/intraventricular hemorrhage
    - Craniotomy
    - Timing of craniotomy
5. Withdrawal of technological support
6. Prevention of recurrent ICH
    - Treatment of hypertension
    - Modification of lifestyle risks: smoking, alcohol use, cocaine use

MAJOR OUTCOMES CONSIDERED

- Neurologic deterioration
- Morbidity, including deep vein thrombosis, pulmonary embolism, rebleeding
- Functional outcome
- Mortality
- Adverse events associated with therapy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A formal literature search of Medline was performed through the end date of August 2006. The results of this search were complemented by additional articles on related issues known to the writing committee.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Therapeutic Recommendation

Level of Evidence A: Data derived from multiple randomized clinical trials

Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies

Level of Evidence C: Consensus opinion of experts

Diagnostic Recommendation

Level of Evidence A: Data derived from multiple prospective cohort studies employing a reference standard applied by a masked evaluator

Level of Evidence B: Data derived from a single grade A study or 1 or more case–control studies or studies employing a reference standard applied by an unmasked evaluator

Level of Evidence C: Consensus opinion of experts

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Data were synthesized with the use of evidence tables. The American Heart Association Stroke Council's Levels of Evidence grading algorithm was used to grade each recommendation.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Class I Conditions for which there is evidence for and/or general agreement that the procedure or treatment is useful and effective

Class II Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment

Class IIa The weight of evidence or opinion is in favor of the procedure or treatment

Class IIb Usefulness/efficacy is less well established by evidence or opinion

Class III Conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases may be harmful

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

A prerelease review of the draft guideline was performed by 5 expert peer reviewers and by the members of the Stroke Council Leadership Committee.

This guideline was approved by the American Heart Association Science Advisory and Coordinating Committee on April 4, 2007.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the recommendation classes (**I, II, III**) and levels of evidence (**A, B, C**) are provided at the end of the "Major Recommendations" field.

Recommendations for Emergency Diagnosis and Assessment of Intracerebral Hemorrhage (ICH)

Class I

1. ICH is a medical emergency, with frequent early, ongoing bleeding and progressive deterioration, severe clinical deficits, and subsequent high mortality and morbidity rates, and it should be promptly recognized and diagnosed (***Class I, Level of Evidence A***).
2. Computed tomography (CT) and magnetic resonance are each first-choice initial imaging options (***Class I, Level of Evidence A***); in patients with contraindications to magnetic resonance, CT should be obtained (***Class I, Level of Evidence A***).

Recommendations for Initial Medical Therapy

Class I

1. Monitoring and management of patients with an ICH should take place in an intensive care unit setting because of the acuity of the condition, frequent elevations in intracranial pressure (ICP) and blood pressure, frequent need for intubation and assisted ventilation, and multiple complicating medical issues (***Class I, Level of Evidence B***).
2. Appropriate antiepileptic therapy should always be used for treatment of clinical seizures in patients with ICH (***Class I, Level of Evidence B***).
3. It is generally agreed that sources of fever should be treated and antipyretic medications should be administered to lower temperature in febrile patients with stroke (***Class I, Level of Evidence C***).
4. As for patients with ischemic stroke, (See the National Guideline Clearinghouse (NGC) summary of the American Stroke Association Guidelines for the Early Management of Adults with Ischemic Stroke) early mobilization and rehabilitation are recommended in patients with ICH who are clinically stable (***Class I, Level of Evidence C***).

Class II

1. Treatment of elevated ICP should include a balanced and graded approach that begins with simple measures, such as elevation of the head of the bed and analgesia and sedation. More aggressive therapies to decrease elevated ICP, such as osmotic diuretics (mannitol and hypertonic saline solution), drainage of cerebrospinal fluid (CSF) via ventricular catheter, neuromuscular blockade, and hyperventilation, generally require concomitant monitoring of ICP and blood pressure with a goal to maintain cerebral perfusion pressure (CPP) >70 mm Hg (***Class IIa, Level of Evidence B***).
2. Evidence indicates that persistent hyperglycemia (>140 mg/dL) during the first 24 hours after stroke is associated with poor outcomes, and thus it is generally agreed that hyperglycemia should be treated in patients with acute stroke. Guidelines for ischemic stroke suggest that elevated glucose concentrations (>185 mg/dL and possibly >140 mg/dL) probably should trigger administration of insulin, similar to the procedure in other acute situations accompanied by hyperglycemia. Use of these guidelines for ICH as well is reasonable. The results of ongoing research should clarify the management of hyperglycemia after stroke (***Class IIa, Level of Evidence C***).

3. Until ongoing clinical trials of blood pressure intervention for ICH are completed, physicians must manage blood pressure on the basis of the present incomplete evidence. Current suggested recommendations for target blood pressures in various situations and potential medications are listed in the tables below and may be considered (***Class IIb, Level of Evidence C***).

Table: Intravenous Medications That May Be Considered for Control of Elevated Blood Pressure in Patients With ICH

Drug	Intravenous Bolus Dose	Continuous Infusion Rate
Labetalol	5 to 20 mg every 15 min	2 mg/min (maximum 300 mg/d)
Nicardipine	NA	5 to 15 mg/h
Esmolol	250 micrograms/kg IVP loading dose	25 to 300 micrograms · kg $^{-1}$ · min^{-1}
Enalapril	1.25 to 5 mg IVP every 6 h*	NA
Hydralazine	5 to 20 mg IVP every 30 min	1.5 to 5 micrograms · kg $^{-1}$ · min^{-1}
Nipride	NA	0.1 to 10 micrograms · kg $^{-1}$ · min^{-1}
Nitroglycerin	NA	20 to 400 micrograms/min

IVP indicates intravenous push; NA, not applicable.

*Because of the risk of precipitous blood pressure lowering, the enalapril first test dose should be 0.625 mg.

Table: Suggested Recommended Guidelines for Treating Elevated Blood Pressure in Spontaneous ICH

1. If SBP is >200 mm Hg or MAP is >150 mm Hg, then consider aggressive reduction of blood pressure with continuous intravenous infusion, with frequent blood pressure monitoring every 5 minutes.
2. If SBP is >180 mm Hg or MAP is >130 mm Hg and there is evidence of or suspicion of elevated ICP, then consider monitoring ICP and reducing blood pressure using intermittent or continuous intravenous medications to keep cerebral perfusion pressure >60 to 80 mm Hg.
3. If SBP is >180 mm Hg or MAP is >130 mm Hg and there is not evidence of or suspicion of elevated ICP, then consider a modest reduction of blood pressure (e.g., MAP of 110 mm Hg or target blood pressure of 160/90 mm Hg) using intermittent or continuous intravenous medications to control blood pressure, and clinically reexamine the patient every 15 minutes.

SBP indicates systolic blood pressure; MAP, mean arterial pressure.

4. Treatment with recombinant activated factor VII (rFVIIa) within the first 3 to 4 hours after onset to slow progression of bleeding has shown promise in one moderate-sized phase II trial; however, the efficacy and safety of this treatment must be confirmed in phase III trials before its use in patients with ICH can be recommended outside of a clinical trial (***Class IIb, Level of Evidence B***).

5. A brief period of prophylactic antiepileptic therapy soon after ICH onset may reduce the risk of early seizures in patients with lobar hemorrhage (***Class IIb, Level of Evidence C***).

Recommendations for Prevention of Deep Vein Thrombosis and Pulmonary Embolism

Class I

1. Patients with acute primary ICH and hemiparesis/hemiplegia should have intermittent pneumatic compression for prevention of venous thromboembolism (***Class I, Level of Evidence B***).
2. Treatment of hypertension should always be part of long-term therapy because such therapy decreases the risk of recurrent ICH (***Class I, Level of Evidence B***).

Class II

1. After documentation of cessation of bleeding, low-dose subcutaneous low-molecular-weight heparin or unfractionated heparin may be considered in patients with hemiplegia after 3 to 4 days from onset (***Class IIb, Level of Evidence B***).
2. Patients with an ICH who develop an acute proximal venous thrombosis, particularly those with clinical or subclinical pulmonary emboli, should be considered for acute placement of a vena cava filter (***Class IIb, Level of Evidence C***).
3. The decision to add long-term antithrombotic therapy several weeks or more after placement of a vena cava filter must take into consideration the likely cause of the hemorrhage (amyloid [higher risk of recurrent ICH] versus hypertension), associated conditions with increased arterial thrombotic risk (e.g., atrial fibrillation), and the overall health and mobility of the patient (***Class IIb, Level of Evidence B***).

Recommendations for the Management of ICH Related to Coagulation and Fibrinolysis

Class I

1. Protamine sulfate should be used to reverse heparin-associated ICH, with the dose depending on the time from cessation of heparin (***Class I, Level of Evidence B***).
2. Patients with warfarin-associated ICH should be treated with intravenous vitamin K to reverse the effects of warfarin and with treatment to replace clotting factors (***Class I, Level of Evidence B***).

Class II

1. Prothrombin complex concentrate, factor IX complex concentrate, and rFVIIa normalize the laboratory elevation of the international normalized ratio (INR) very rapidly and with lower volumes of fluid than fresh frozen plasma (FFP) but with greater potential of thromboembolism. FFP is another potential

choice but is associated with greater volumes and much longer infusion times (***Class IIb, Level of Evidence B***).
2. The decision to restart antithrombotic therapy after ICH related to antithrombotic therapy depends on the risk of subsequent arterial or venous thromboembolism, the risk of recurrent ICH, and the overall state of the patient. For patients with a comparatively lower risk of cerebral infarction (e.g., AF without prior ischemic stroke) and a higher risk of amyloid angiopathy (e.g., elderly patients with lobar ICH) or with very poor overall neurological function, an antiplatelet agent may be an overall better choice for prevention of ischemic stroke than warfarin. In patients with a very high risk of thromboembolism in whom restarting warfarin is considered, warfarin therapy may be restarted at 7 to 10 days after onset of the original ICH (***Class IIb, Level of Evidence B***).
3. Treatment of patients with ICH related to thrombolytic therapy includes urgent empirical therapies to replace clotting factors and platelets (***Class IIb, Level of Evidence B***).

Recommendations for Surgical Approaches

Class I

1. Patients with cerebellar hemorrhage >3 cm who are deteriorating neurologically or who have brain stem compression and/or hydrocephalus from ventricular obstruction should have surgical removal of the hemorrhage as soon as possible (***Class I, Level of Evidence B***).

Class II

1. Although stereotactic infusion of urokinase into the clot cavity within 72 hours of ictus apparently reduces the clot burden and risk of death, rebleeding is more common, and functional outcome is not improved; therefore, its usefulness is unknown (***Class IIb, Level of Evidence B***).
2. Although theoretically attractive, the usefulness of minimally invasive clot evacuation utilizing a variety of mechanical devices and/or endoscopy awaits further testing in clinical trials; therefore, its current usefulness is unknown (***Class IIb, Level of Evidence B***).
3. For patients presenting with lobar clots within 1 cm of the surface, evacuation of supratentorial ICH by standard craniotomy might be considered (***Class IIb, Level of Evidence B***).

Class III

1. The routine evacuation of supratentorial ICH by standard craniotomy within 96 hours of ictus is not recommended (***Class III, Level of Evidence A***). (See possible Class II exception above for patients presenting with lobar clots within 1 cm of the surface.)

Recommendations for Timing of Surgery

Class II

1. No clear evidence at present indicates that ultra-early craniotomy improves functional outcome or mortality rate. Operative removal within 12 hours, particularly when performed by less-invasive methods, has the most supportive evidence, but the number of subjects treated within this window is very small (***Class IIb, Level of Evidence B***). Very early craniotomy may be associated with an increased risk of recurrent bleeding (***Class IIb, Level of Evidence B***).

Class III

1. Delayed evacuation by craniotomy appears to offer little if any benefit with a fairly high degree of certainty. In those patients presenting in coma with deep hemorrhages, removal of ICH by craniotomy may actually worsen outcome and is not recommended (***Class III, Level of Evidence A***).

Recommendation for Decompressive Craniectomy

Class II

1. Too few data currently exist to comment on the potential of decompressive craniectomy to improve outcome in ICH (***Class IIb, Level of Evidence C***).

Recommendation for Withdrawal of Technological Support

Class II

1. We recommend careful consideration of aggressive full care during the first 24 hours after ICH onset and postponement of new do not resuscitate (DNR) orders during that time (***Class IIb, Level of Evidence B***). Patients with previous DNR orders are not included in this recommendation. In all cases, physicians and nurses caring for ICH patients who are given DNR status should be reminded that the designation relates only to the circumstance of cardiopulmonary arrest and that patients should receive all other appropriate medical and surgical interventions.

Recommendations for Prevention of Recurrent ICH

Class I

1. Treating hypertension in the nonacute setting is the most important step to reduce the risk of ICH and probably recurrent ICH as well (***Class I, Level of Evidence A***).
2. Smoking, heavy alcohol use, and cocaine use are risk factors for ICH, and discontinuation should be recommended for prevention of ICH recurrence (***Class I, Level of Evidence B***).

Definitions:

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Therapeutic Recommendation

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Level of Evidence C: Consensus opinion of experts

Diagnostic Recommendation

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Level of Evidence B: Data derived from a single grade A study or 1 or more case–control studies or studies employing a reference standard applied by an unmasked evaluator

Level of Evidence C: Consensus opinion of experts

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Early diagnosis of and appropriate use of medical and surgical therapies for intracerebral hemorrhage

POTENTIAL HARMS

- *Recombinant activated factor VII* is associated with serious thromboembolic adverse events, mainly myocardial and cerebral infarction.
- Attempts to control blood pressure must be balanced with the theoretical risks of inducing cerebral ischemia in the edematous region that surrounds the hemorrhage.
- The principal risks of ventriculostomy are infection and hemorrhage.
- Neuromuscular blockade is associated with an increased risk of complications: such as pneumonia and sepsis, and can obscure seizure activity.
- The major problems associated with *mannitol* administration are hypovolemia and the induction of a hyperosmotic state.
- After a patient has been hyperventilated for >6 hours, rapid normalization of arterial PC_{O2} can cause a significant rebound increase in intracranial pressure (ICP).
- *Prothrombin complex concentrate* is associated with the risk of inducing thromboembolic complications, ranging from superficial thrombophlebitis, deep vein thrombosis and pulmonary embolism, and arterial thrombosis to disseminated intravascular coagulation.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Tool Kits

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Safety
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Broderick J, Connolly S, Feldmann E, Hanley D, Kase C, Krieger D, Mayberg M, Morgenstern L, Ogilvy CS, Vespa P, Zuccarello M, American Heart Association, American Stroke Association Stroke Council, High Blood Pressure Research Council, Quality of Care and Outcomes in Research Interdisciplinary Working Group. Guidelines for the management of spontaneous intracerebral hemorrhage in adults: 2007 update. Stroke 2007 Jun;38(6):2001-23. [204 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Jun

GUIDELINE DEVELOPER(S)

American Heart Association - Professional Association
American Stroke Association - Disease Specific Society

SOURCE(S) OF FUNDING

American Heart Association

GUIDELINE COMMITTEE

American Heart Association/American Stroke Association Stroke Council

High Blood Pressure Research Council

Quality of Care and Outcomes in Research Interdisciplinary Working Group

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest (see disclosure tables below).

Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Ownership Interest	Consultant/ Boa
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Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Ownership Interest	Consultant/ Boa
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Paul Vespa	University of California, Los Angeles	None	None	PDL	None	The Medicine Company
Mario Zuccarello	Mayfield Clinic	None	None	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit.

Reviewer Disclosures

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Donald D. Heistad	University of Iowa College of Medicine	NIH	None	None	None	None	None
Edward C. Jauch	University of Cincinnati College of Medicine	Biosite	None	Boehringer Ingelheim	None	None	AstraZeneca; B Genentech; Joh Johnson; Novo
Stephan Mayer	Columbia University	Novo Nordisk	None	Novo Nordisk; PDL BioPharma	None	None	Novo Nordisk; I BioPharma

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit.

GUIDELINE STATUS

This is the current release of the guideline.

It is intended that this guideline be fully updated in 3 years' time.

GUIDELINE AVAILABILITY

Electronic copies: Available from the American Heart Association Web site.

Print copies: Available from the American Heart Association, Public Information, 7272 Greenville Ave, Dallas, TX 75231-4596; Phone: 800-242-8721

AVAILABILITY OF COMPANION DOCUMENTS

Get With the Guidelines (GWTG) provides disease-specific process documents and tools for in-house quality improvement. See the American Heart Association Web site for more information. See the related QualityTool summary on the Health Care Innovations Exchange Web site for this related tool set.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI Institute on July 24, 2007. The information was verified by the guideline developer on August 23, 2007. This summary was updated by ECRI Institute on March 14, 2008 following the updated FDA advisory on heparin sodium injection.

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